

超音波檢測生物可分解性高分子之性質

An Ultrasonic Technique for Characterization of Biodegradable Polymers

*王希俊(H. Wang), **張文基(W. V. Chang), ***霍華·溫納(H. Winet)

摘 要

生物可分解性高分子除了應用於藥物控制釋放及骨科復健植入也是一種具有環保特性的被印體材料，本研究應用超音波檢測技術來量測生物可分解性高分子浸置於水中不同時間後的裂解特性，二千萬周率之縱波由超音波轉換器產生後穿透過高分子材料並由感測器接收及數位化，快速傅立葉轉換及交錯相關係數法等數位訊號處理技術將數位化的波形轉換，並計算超音波在分子中的波速及衰減係數，結果顯示超音波的波速在分子裂解過程中降低三分之一而衰減係數則增加四倍，故超音波檢測技術是有用的工具來量測與鑑定生物可分解性高分子材料的裂解特性。

Abstract

An ultrasonic technique was used to measure material property change during hydrolytic degradation of a biodegradable copolymer, 50/50 poly(D,L-lactide-co-glycolide). Six groups of 3 copolymer buttons were immersed in 60°C distilled water for 0, 1.5, 3.0, 6.0, 10.0 and 24.0 hours. A longitudinal wave generated by a 20 MHz transducer and a pulser/receiver card was directed perpendicularly to the copolymer disk at 20°C. The reflected signals coming back to transducer were recorded and saved through a data acquisition board. The longitudinal wave speeds and attenuation coefficients of the disks undergoing various exposures to a water bath were calculated by the cross-correlation method and fast Fourier transformation (FFT) of the digitized waveform data. The wave speed decreased by a factor of one third and the attenuation coefficient increased up to four times within 24 hours in the 60°C water bath. The results suggest that the ultrasonic technique provides a useful method for the study of hydrolytic degradation of poly(D,L-lactide-co-glycolide) in a non-destructive manner.

關 鍵 詞：縱波；波速；衰減係數；生物可分解性高分子，

Keywords: longitudinal wave, wave speed, attenuation coefficient, poly(D,L-lactide-co-glycolide)

*王希俊：台灣師範大學圖文傳播學系，National Taiwan Normal University, Taipei, Taiwan

**張文基：美國南加州大學化學工程系，Department of Chemical Engineering, University of Southern California

***霍華·溫納：美國南加州大學骨科及生醫工程，美國南加州大學骨科醫院，Department of Orthopaedics and Biomedical Engineering and Orthopaedic Hospital, University of Southern California, Los Angeles, California, USA

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INTRODUCTION

Biodegradable polymers have been used for bone fixation because they possess some unique characteristics like providing initial strength, which is gradually lost during bone healing, and eliminating the need for hardware removal operations [1]. However, it is not easy to study the biodegradation of these polymers in situ. Ultrasound has been applied to study various tissues in a non-destructive manner [2,3]. In this study, an ultrasonic technique for monitoring the biodegradation of poly(D, L-lactide-co-glycolide) in vitro is presented.

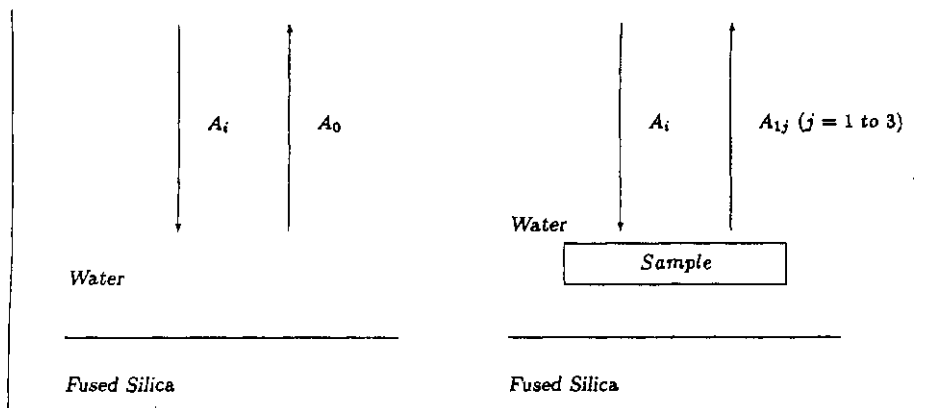
MATERIALS AND METHODS

Granules of 50/50 poly(D,L-lactide-co-glycolide) (batch # 32-138) were provided by PURAC Biochem (The Netherlands). Intrinsic viscosity was measured with a capillary Ostwald viscometer, yielding a value of 0.63dl/g in chloroform at 23°C. A copolymer disk 63mm in diameter and 0.54mm thick was made by compression molding at 140°C. A trephine was used to cut the specimen into small disks 8mm in diameter and 0.54mm thick. Six groups of 3 copolymer disks, 18 in total, were utilized. Five groups were immersed in 60°C distilled water for 1.5, 3.0, 6.0, 10.0 and 24.0 hours. The remaining group was used as a control. After these copolymer discs had been submerged in 60°C water from 0 to 24 hours, they were transferred to another water bath for ultrasonic measurement at 20°C.

A pulser/receiver card and a longitudinal transducer with nominal fre-

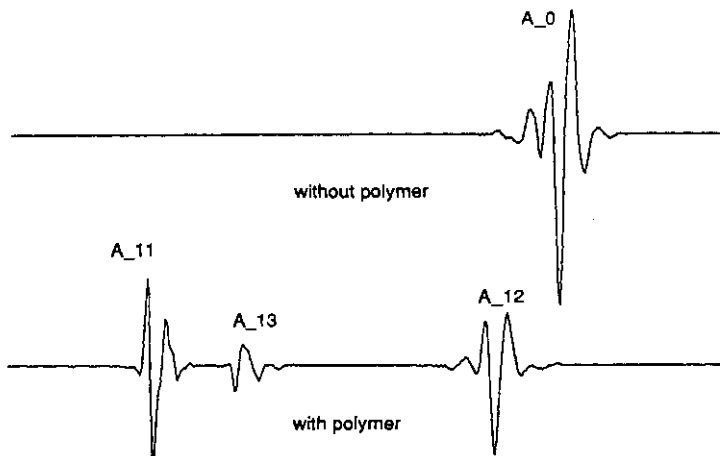
quency of 20MHz were applied to generate and detect the ultrasonic waves. Analog signals were digitized by a data acquisition card and displayed on a digital oscilloscope. The experimental setup is shown in (Fig. 1). . The longi-

Figure 1: Schematic graph of a longitudinal wave normally incident on specimen above a highly reflecting fused silica plate immersed in a water bath. Where A_i is the amplitude of the incident wave, and A_0 and A_{1j} are the amplitude of reflected waves while sample is not present (left) and is present (right), respectively.



tudinal wave was normally incident on the specimen. Where there was no specimen, one reflection ($A_0(t)$) (from the water-fused silica interface) was observed. Where there was a specimen, three peak signals ($A_{11}(t)$, $A_{12}(t)$ and $A_{13}(t)$) were observed (Fig. 2). $A_{11}(t)$ and $A_{13}(t)$ were reflected from the upper and lower water-specimen interfaces, respectively. $A_{12}(t)$ was reflect-

Figure 2: The waveforms of the reflected signals while the sample is not present and is present, respectively. The arrival times for the four signals are t_0 , t_{11} , t_{13} and t_{12} , respectively.



ed from the water-substrate interface. All the ultrasonic measurements were conducted at 20°C.

At each measurement, the arrival times for four signals, t_0 , t_{11} , t_{12} and t_{13} , were obtained, as shown Fig. 2. The thickness, d , of the copolymer disk was determined from:(1)

$$(1) \quad d = ((t_0 - t_{11}) - (t_{12} - t_{13}))v_w / 2$$

where v_w is the wave speed in water (1483 m/sec at 20°C[4]). The longitudinal wave speed, v_p , of the copolymer was derived from(2)

$$(2) \quad v_p = \frac{(t_0 - t_{11}) - (t_{12} - t_{13})}{t_{13} - t_{11}} \cdot v_w$$

The attenuation coefficient (α) is defined as [5]:(3)

$$(3) \quad \alpha = \frac{1}{2d} \ln \frac{(1 - R_{wp}^2)}{A_{12}/A_0}$$

where R_{wp} is the reflection coefficient of longitudinal waves striking the water-copolymer interface. R_{wp} can be written as[4]:(4)

$$(4) \quad R_{wp} = \frac{Z_p - Z_w}{Z_p + Z_w} = \frac{Z_s - Z_w}{Z_s + Z_w} \cdot \frac{A_{11}}{A_0}$$

where Z_s and Z_w are, respectively, the mechanical impedances of reflecting surface (fused silica) and water; these values are known[4].

All waveforms were digitized and stored in binary format by a personal computer. The cross correlation method and fast Fourier transformation (FFT) were used to analyze the digitized data and calculate wave speed and attenuation coefficient of each sample.

Since $A_0(t)$, $A_{11}(t)$, $A_{12}(t)$ and $A_{13}(t)$ were in digital data format, precise

measures of $t_0 - t_{11}$, $t_{12} - t_{13}$ and $t_{13} - t_{11}$ were sufficient for calculating wave speed from Eq. 2. The cross-correlation function[6,7,2] utilized was:(5)

$$(5) \quad C(T) = \int_0^{\infty} A_{11}(t) \cdot A_0(t+T)dt$$

At $T = T_{\max}^c$ the cross correlation function, C_{\max} , is a maximum and $T_{\max}^c = t_0 - t_{11}$. Similarly, $t_{12} - t_{13}$ and $t_{13} - t_{11}$ were determined.

By plugging values of $t_0 - t_{11}$, $t_{12} - t_{13}$ and $t_{13} - t_{11}$ into Eq. 2, the wave speed of the sample can be calculated. Under these experimental conditions, a pulse was generated from a longitudinal transducer with nominal frequency 20MHz. Due to the dispersive nature of a pulsed wave, this calculated wave speed is group velocity which tends to be determined by the major components around the peak frequency (about 8.5MHz) of reflected signals[4]. In order to get attenuation coefficient at peak frequency, all $A_0(t)$, $A_{11}(t)$, $A_{12}(t)$, and $A_{13}(t)$ values were transformed from time domain to frequency domain by fast Fourier transformation (FFT):(6)

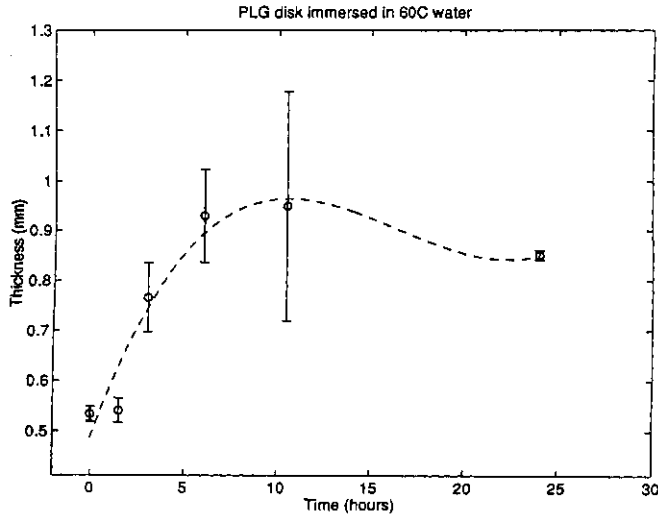
$$(6) \quad A_0(t) \text{ and } A_{1j}(t) \xrightarrow{\text{FFT}} A_0(f) \text{ and } A_{1j}(f) \quad j=1 \text{ to } 3$$

From Eq. 3 and Eq. 4, the important parameters for determining longitudinal wave attenuation are $A_{12}(f)/A_0(f)$ and $A_{11}(f)/A_0(f)$. Calculated values are based on peak frequency of the reflected signals.

RESULTS AND DISCUSSION

Thickness, wave speed and attenuation coefficient were measured for the samples immersed in 60°C water from 0 to 24 hours. Fig. 3 shows that the thickness of the copolymer increased during the first 10 hours and then decreased gradually. The increase might be due to copolymer swelling which has been observed[8]. As shown in Fig. 4, the longer a specimen stayed in a hot water bath, the slower waves traveled through it. Since the

Figure 3: The thickness of copolymer button changes with time.



ultrasonic waves are elastic waves, this result implies a loss of specimen mechanical strength. As shown in Fig. 5, the attenuation coefficient increased with time. The material absorbed more wave energy as it became more viscous. At the end of the experiment, it lost integrity and looked like thickened starch. Between 5 hours and 24 hours, both the wave speed and attenuation coefficient show rapid changes suggesting a transition from a glassy state to a viscous state. Data dispersion at 10 hours is quite large for the parameters shown in Figures 3-5. It suggests that the extent of biodegradation inside these disks is not homogeneous at this stage. Note

Figure 4: The change of wave speed at 20°C in copolymer buttons which underwent different intervals in 60°C water bath.

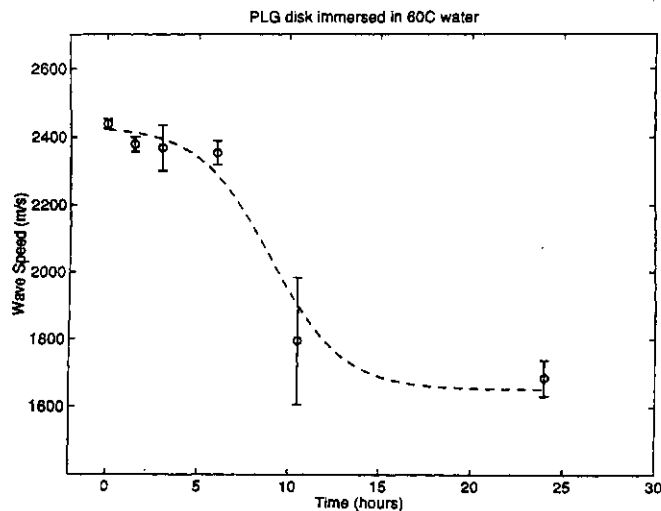
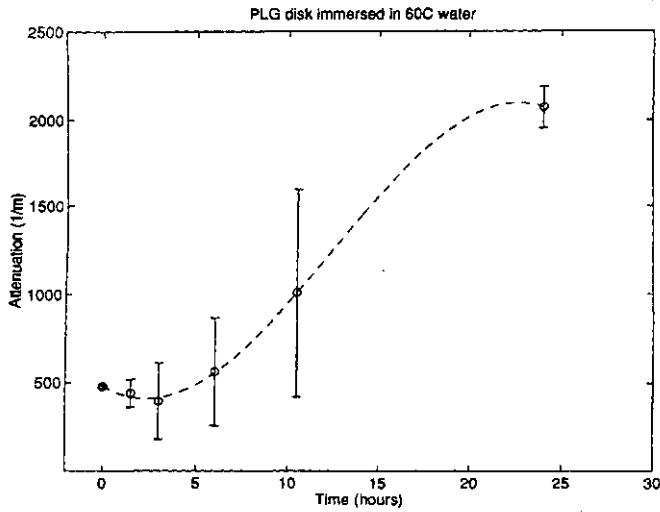


Figure 5: The change of attenuation coefficient at 20°C in copolymer buttons which underwent different intervals in 60°C water bath.



that erosion is not complete after 24 hours in the water bath.

This study was not performed at body temperature (37°C) and in phosphate buffer solution (PBS), as would be recommended for the future studies. Its purpose was to demonstrate the feasibility of ultrasonic technique for characterization of biodegradable materials. The copolymer utilized is a bulk eroder[9]. Surface eroding polymers would probably exhibit different ultrasonic patterns.

Frequency selection is a major determinant of the utility of ultrasonic measurements. Although higher frequencies can achieve higher resolution, penetration depth would decrease in an inverse relationship. It may be possible to apply the ultrasonic technique to measure copolymer erosion in an in vivo implant such as the optical bone-chamber which carries the polymer in a 100 μ m-thick compartment. In this case, the ultrasonic frequency should increase up to 50-100MHz to ensure acceptable resolution. In order to achieve adequate ultrasonic wave penetration depth for future in vivo studies of centimeter thick implant copolymer, ultrasonic wave frequencies would have to be reduced to up to 2-5MHz.

References

- [1] Sander T. Resorbable polymers for the bone surgeon. Portland Bone Symposium, Oregon Health Sciences University, Portland, Oregon, 1995; pages 647-653.
- [2] Daft CMW, Briggs GAD. Wideband acoustic microscopy of tissue, IEEE Trans. Ultrason. Ferroelect. Freq. Contr. 1989; 36(2): 258-263.
- [3] Madsen EL, Sathoff HJ, Zagzebski JA. Ultrasonic shear wave properties of soft tissues and tissuelike materials. J. Acoust. Soc. Am. 1983; 74:1346-1355.
- [4] Bray DE, Stanley RK. Nondestructive Evaluation, Chap 5, Elastic Wave Propagation. McGraw-Hill Book Company, New York, 1989.
- [5] McClements DJ, Fairley P. Frequency scanning ultrasonic pulse echo reflectometer. Ultrason. 1992; 30(6):403-405.
- [6] Ziola SM, Gorman MR. Source location in thin plates using cross-correlation. J. Acoust. Soc. Am. 1991; 90:2551-6.
- [7] Wu TT, Chiu ST. On the propagation of horizontally polarized shear waves in a thin composite laminate plate. Ultrason. 1992; 30(1): 60-64.
- [8] Winet H, Hollinger JO. Incorporation of polylactide-polyglycolide in a cortical defect: Neoosteogenesis in a bone chamber. J. Biomed. Mat. Res. 1993; 27:667-676.
- [9] Tamada JA, Langer R. Erosion kinetics of hydrolytically degradable polymers. Proc. Natl. Acad. Sci. USA 1993; 90:552-556.